

REMARKS/ARGUMENTS

Applicants received and reviewed an Office Action dated July 1, 2003. Applicants request entry of this Amendment in response and reconsideration of the rejection of the claims.

Applicants canceled claims 63-65, 99 and 100, without prejudice or disclaimer. Applicants reserve the right to pursue any subject matter of these claims in a continuation application.

Applicants have amended claims 51, 66, 79-86, 101, 110, 111 and 117-120. The amended claims are supported throughout the specification.

No new claims have been added.

Rejections

35 U.S.C. § 112, First Paragraph

Claims 51-66, 69-102 and 105-146 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it was most nearly connected, to make and/or use the invention. Examiner first indicates that as written the claims were “broadly written” and not enabled. Specifically, the Examiner indicated that the term “ungulate” is a broad term that encompasses a wide variety of animals that would not be considered a single species. Citing the Encyclopedia Britannica, the Examiner indicates that an ungulate is “generally any hoofed animal.” Applicants respectfully point out to the Examiner that claims 51 and 86 have been amended to specifically indicate which ungulate animals the claims pertain to. These amendments are supported in the specification, specifically on page 15, lines 4-11; page

18, lines 26-28; page 19, lines 1 and 2, as well as the examples. Applicants maintain that the claims as currently amended overcome this rejection.

The Examiner next argues that the state of cross-species nuclear transfer is unpredictable. Applicants respectfully traverse this requirement and cite the following references as support. Applicants cite the work of Chen et al. (Cell Research (2003)13(4); 251-263) which disclose that rabbit oocyte cytoplasm was used as a means to reprogram human somatic cell nuclei. They demonstrate that cells derived from this reprogramming possess the properties of conventional human embryonic stem cells (ES) in retaining the normal karyotype and that the cells are capable of multilineage cellular differentiation. Chen et al. disclose the fusion of human fibroblasts with rabbit oocytes as a successful means of generating nuclear transfer units from different species. In addition, the work of Loi et al. (2001, Nature Biotechnology 19:962-964) disclose the nuclear transfer from granulosa cells collected from two female mouflons found dead in a pasture into enucleated sheep oocytes and the subsequent production of viable offspring. In addition, Applicants also cite an abstract submitted to the IETS Conference describing the production of a banteng calf produced by the nuclear transfer of a banteng cell into a sheep oocyte. Copies of all cited references are enclosed for the Examiner's convenience as well as included on the enclosed PTO-1449 Form.

Thus, Applicant's can point to at least three critical pieces of information in support of the argument that the specification would not lead one skilled in the art to undue experimentation with regard to the methodology claimed. First, the Applicant's own data showing a successful *Bos taurus/Bos gaurus* nuclear transfer contained within the specification; a successful *Bos javanicus* to *Bos taurus* nuclear transfer (San Diego Zoo report); as well as the *Ovis/Ovis* nuclear transfer as described in Loi et al. Applicants respectfully point out that the cited art clearly

demonstrates that cross species nuclear transfer is successful and predictable. This in addition to the successful example indicated in the current specification would argue against the claims by the Examiner that the state of the art of cross-species nuclear transfer is unpredictable.

Furthermore, not only do the references cited show that fully-formed animals can be produced by the claimed methodology, but Chen et al. provide evidence of the totipotency of the cells of the nuclear transfer units produced.

The Examiner also states that heteroplasmy is only seen if closely related species are utilized for nuclear transfer technology, whereas if different species are used, xenomitochondrial cybrids are generated. Chen (cited above) showed that the nuclear transfer units produced in the human/rabbit transfer contained the primate DNA in combination with rabbit mitochondrial DNA (p. 254, second column, bottom) thus showing that at least some of the mitochondrial DNA is present from the donor cell. However, the evidence cited in the preceding paragraphs clearly demonstrates the ability of the claimed methodology to produce viable offspring from non-identical species transfers without regard whether the offspring is heteroplasmic or not.

The Examiner also cites the work of Gardner et al. (Int. J. Dev. Bio., 41, 235-243 (1997)) as disclosing that embryonic stem-like cells obtained from several species “have been shown to be able to support normal development when transplanted into enucleated oocytes” but that this does not “constitute proof that the cells themselves retain totipotency.” Applicants submit that Gardner et al. discloses a review of what purportedly is the state of the art of the development of embryonic stem cells and related technology. Applicants assert that this reference is not a relevant reference. Firstly, this reference details the state of the art as of 1997 and references indicated in Gardner et al., which disclose work from ungulates reflect the state of the art from 1992 to 1996 (page 236, table 1). Applicants assert that this reference does not disclose or is

relevant to the teachings of the current specification, which disclose the successful production of a fully formed animal from a cross-species nuclear transfer.

The Examiner also cites the work of Hammer et al. (Theriogenology, 55:1447-1455 (2001)) as teaching the interspecies transfer between *Bos gaurus* and *Bos taurus* as representing the state of the art describing the unpredictability of interspecies transfers. Again, Applicants respectfully assert that this reference is not relevant. Hammer et al. disclose the effects of interspecies transfer of in vitro fertilization-derived embryos. Hammer et al. does not disclose the production of nuclear transfer units as described in the current specification. Therefore any conclusions in Hammer et al. relating to interspecies transfer and the production of embryonic stem cells is irrelevant to the current argument.

The Examiner further argues that with respect to the claimed “embryonic cells” of claims 79-85, the specification fails to enable the production of embryonic or stem-like cells. Applicants respectfully point out that claims 79-85, 110, 111, and 117-120 have been amended to remove the term “embryonic.”

Applicants maintain that the specification does not lead one skilled in the art to undue experimentation necessary to practice the invention disclosed within the specification. Applicants as argued above maintain that the state of the art is not unpredictable and that the specification leads to the development of a nuclear transfer unit, which can lead to viable offspring. Applicants therefore respectfully request withdrawal of these rejections.

35 U.S.C. § 112, Second Paragraph

Claims 51-83, 86 and 117 are described by the Examiner as vague and are rejected under 35 U.S.C. §112 as failing to point out and distinctly claim the subject matter which the

Applicants regard as the invention. Applicants respectfully traverse this rejection. Applicants point out that with the amendments entered within the attached response, the term “ungulate species” has been amended to more accurately claim the invention. Applicants therefore respectfully request withdrawal of this rejection.

CONCLUSION

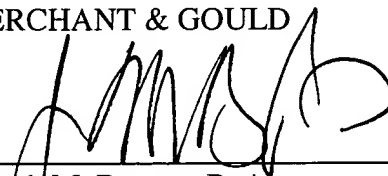
Applicants respectfully submit that the foregoing Amendment and Response place this application in condition for allowance. If the Examiner believes that there are any issues that can be resolved by a telephone conference, or that there are any informalities that can be corrected by an Examiner’s amendment, please call the undersigned at 404.954.5044.

Appl. No. 09685,061
Amdt. Dated January 2, 2004
Reply to Office Action of July 1, 2003

No fees are believed due; however the commissioner is authorized to charge any fee due or refund any credit to Deposit Account No. 13-2725.

Respectfully submitted,

MERCHANT & GOULD

A handwritten signature in black ink, appearing to read 'JMBP', written over a horizontal line.

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